

REMARKS

For the Examiner's convenience, Applicants will now address stated issues and grounds for rejection of the pending claims under the appropriate subheadings.

Amendments to the Claims

Claim 1 has been amended to recite that the polydiallylamine polymer is characterized in that the polymer is free of alkylated amine monomers. Support for the amendment to Claim 1 can be found, *inter alia*, in Examples 1-15 and Formula I and II at page 4 of the specification. Claim 1 has also been amended to delete the phrase "of an effective amount".

Claim 3 has been amended to further clarify that the purpose of epichlorohydrin in the claimed invention is as a crosslinking agent. Support for the amendment to Claim 3 can be found at page 8 lines 20-22 of the specification.

No new matter has been added as a result of the amendments made herein.

Rejection of Claims 1-8 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected Claim 1-8 under 35 U.S.C § 112, Second Paragraph as being indefinite for failing to point out and distinctly claim the subject matter which applicants regard as the invention. In particular, the Examiner asserted that the terms "substantially" and "effective amount" render Claim 1 vague.

Claim 1 has been amended to no longer recite the term "substantially." However, Applicants respectfully disagree with the Examiner but have amended the claim to further prosecution. The claim now recites that the polydiallylamine homopolymer is free of alkylated amine monomers. In addition, Claim 1 has been amended to no longer recite the phrase "effective amount."

The Examiner has rejected Claim 3 under 35 U.S.C § 112, Second Paragraph as being vague in view of Lukach *et al.*, (U.S. Patent 4,604,217). The Examiner asserted that crosslinking with epichlorohydrin contradicts the alkylated uncrosslinked product obtained in Lukach *et al.* rendering the claim vague. Applicants respectfully disagree.

As a preliminary matter, one of ordinary skill in the art on reading Claim 3, particularly in view of its dependence on Claim 2, would understand that the epichlorohydrin is functioning as a

crosslinking agent. The claim has been amended to further clarify the crosslinking function of the epichlorohydrin in the claimed invention.

Applicants' claims, as amended, are directed to a pharmaceutical composition comprising a unit dosage form of a polydiallylamine homopolymer which is free of alkylated amine monomers, and a pharmaceutically acceptable carrier. The pharmaceutical composition can be used to treat, for example, hypercholesterolemia, atherosclerosis and/or reduction of serum cholesterol.

Lukach *et al.* do not teach a pharmaceutical composition. Rather, Lukach *et al.* teach a gelled aqueous composition comprising a poly(diallylamine)-epihalohydrin resin which is useful in the recovery of oil and gas by fracturing and as a matrix plugging agent in enhanced oil recovery. Lukach *et al.*, use epihalohydrin as a crosslinking agent to covalently bind the polydiallylamine polymers to a distinct anionic or nonionic water soluble polymers to produce the gelled composition of the invention (Column 2 lines 10-13 and 25-31). The alkylated uncrosslinked product referred to by the Examiner (Column 3 line 30 to Column 4 line 54), is an acid stabilized intermediate used for manufacturing of the poly(diallylamine)-epihalohydrin resin. More specifically, Lukach *et al.* first react the polydiallylamine polymer with epihalohydrin. This intermediate is then stored under acidic conditions to prevent the epihalohydrin substituents from binding independent polydiallylamine polymer strands together to form a gel (Column 4 line 39-42). The acid stabilized intermediate is then activated under basic conditions prior to use, to permit the binding of polydiallylamine strands to distinct anionic or nonionic water soluble polymer strands. As such, the resulting gelled formulation is not a polydiallylamine homopolymer and, in fact, Lukach *et al.* attempt to avoid homopolymer formation by storage of the intermediate under acidic conditions. More importantly, the polymer of Lukach is not a pharmaceutical composition.

The Examiner appears to have equated crosslinking and alkylation. However, "crosslinking" and "alkylation" are terms of art, which one of ordinary skill in the art would not construe as the same. That is, crosslinking provides a bridging unit between two independent polymer chains, whereas alkylation provides an alkyl substituent on, for example, the amino nitrogen of a polymer backbone. Applicants' specification clearly teaches that crosslinking and alkylation are distinct (See, for example, page 4 lines 17-18 - page 5 lines 1-4). Therefore, one of

ordinary skill in the art would not find it contradictory to have an alkylated amine polymer which is not crosslinked as in the acid stabilized intermediate of Lukach *et al.* Further, one of ordinary skill in the art would understand from Applicants' specification, and from what is well-known in the art, that a crosslinked amine polymer, in addition to having bridging units connecting individual polymer strands, can be alkylated at the amino nitrogens of the polymer.

Alternatively, an amine polymer which is alkylated at the amino nitrogens would not be considered crosslinked. Therefore although crosslinking and alkylation can both result from a nucleophilic substitution reaction, they are distinct chemical manipulations well-known in the polymer art.

In view of the above, Applicants' invention, as claimed, and the manner of making and using it, are described in such full, clear, concise and exact terms, as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and sets forth the best mode contemplated by the inventor of carrying out his invention. Therefore, the pending claims, particularly as amended, clearly set out the boundaries of the subject matter for which protection is sought. Applicants submit that all pending claims meet the requirements of 35 U.S.C. §112, Second Paragraph. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 1 and 4 Under 35 U.S.C. §102 (b)

The Examiner has rejected Claims 1 and 4 under 35 U.S.C. §102 (b) as being anticipated by Perry *et al.* (US Patent No. 4,659,474). In particular, the Examiner stated that Perry *et al.* teach tablets comprising polydiallylamine derivatives. Applicants respectfully disagree. Applicants' claims are directed to a pharmaceutical composition comprising a unit dosage form of an effective amount of a polydiallylamine homopolymer which is free of alkylated amine monomers and a pharmaceutically acceptable carrier. As set forth in the specification, the pharmaceutical composition can be used, for example, as a bile acid sequestrant for the treatment of hypercholesterolemia, atherosclerosis and/or reduction of serum cholesterol.

Perry *et al.* teach basic polymer membrane supports (e.g., polyacrylonitrile) which can be modified by the deposition of a hydrophilic polymer (e.g., polyethyleneimine) on the membrane and then optionally crosslinked. The polymers are used in ultrafiltration and reverse osmosis

processes for the concentration and purification of liquids. Perry *et al.* do not teach or suggest that the modified polymer membranes are a pharmaceutical composition.

The Examiner notes that Perry *et al.* mention polydiallylamine polymers at Col. 8, line 62) and tablets at Col. 12, line 25. However, the tablets described at Col 12, line 25 of Perry *et al.* are not tablets of polydiallylamine. Rather, the tablets described at Col. 8, line 62 of Perry *et al.* are tablets of the modified filtration membrane (e.g., an acrylonitrile polymer modified by deposition of a polyethyleneimine). Further, at Col 8, line 62, Perry *et al.* teach a long list of hydrophilic polymers which can be used to modify the basic polymer membrane of the filtrations devices described. Clearly, these teaching in Perry *et al.* taken either separately or in combination neither teach nor suggest a pharmaceutical composition comprising a unit dosage form of polydiallylamine homopolymer which is free of alkylation and a pharmaceutically acceptable carrier.

In view of the above, Applicants' claims meet the requirements of 35 U.S.C. §102 (b) and are patentable over the teachings of Perry *et al.* Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,
HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Bonela A. Torrey (45,736) for
Susan M. Abelleira
Registration No. 42,252
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133

Dated: December 8, 2003